

wherein **B** is H, a C<sub>6</sub> or C<sub>10</sub> aryl, C<sub>7-16</sub> aralkyl; Het or (lower alkyl)-Het, all of which optionally substituted with C<sub>1-6</sub> alkyl; C<sub>1-6</sub> alkoxy; C<sub>1-6</sub> alkanoyl; hydroxy; hydroxyalkyl; halo; haloalkyl; nitro; cyano; cyanoalkyl; amino optionally substituted with C<sub>1-6</sub> alkyl; amido; or (lower alkyl)amide;

or **B** is an acyl derivative of formula **R**<sub>4</sub>-C(O)-; a carboxyl derivative of formula **R**<sub>4</sub>-O-C(O)-; an amide derivative of formula **R**<sub>4</sub>-N(**R**<sub>5</sub>)-C(O)-; a thioamide derivative of formula **R**<sub>4</sub>-N(**R**<sub>5</sub>)-C(S)-; or a sulfonyl derivative of formula **R**<sub>4</sub>-SO<sub>2</sub> wherein

**R**<sub>4</sub> is (i) C<sub>1-10</sub> alkyl optionally substituted with carboxyl, C<sub>1-6</sub> alkanoyl, hydroxy, C<sub>1-6</sub> alkoxy, amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl, amido, or (lower alkyl) amide;

(ii) C<sub>3-7</sub> cycloalkyl, C<sub>3-7</sub> cycloalkoxy, or C<sub>4-10</sub> alkylcycloalkyl, all optionally substituted with hydroxy, carboxyl, (C<sub>1-6</sub> alkoxy)carbonyl, amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl, amido, or (lower alkyl) amide;

(iii) amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl; amido; or (lower alkyl)amide;

(iv) C<sub>6</sub> or C<sub>10</sub> aryl or C<sub>7-16</sub> aralkyl, all optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl; or

(v) Het or (lower alkyl)-Het, both optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amido, (lower alkyl) amide, or amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl;

**R**<sub>5</sub> is H or C<sub>1-6</sub> alkyl; with the proviso that when **B** is a carboxyl derivative, an amide derivative or a thioamide derivative, **R**<sub>4</sub> is not a cycloalkoxy;

**Y** is H or C<sub>1-6</sub> alkyl;

**R**<sup>3</sup> is C<sub>1-8</sub> alkyl, C<sub>3-7</sub> cycloalkyl, or C<sub>4-10</sub> alkylcycloalkyl, all optionally substituted with hydroxy, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> thioalkyl, amido, (lower alkyl)amido, C<sub>6</sub> or C<sub>10</sub> aryl, or C<sub>7-16</sub> aralkyl;

**R**<sup>2</sup> is CH<sub>2</sub>-**R**<sub>20</sub>, NH-**R**<sub>20</sub>, O-**R**<sub>20</sub> or S-**R**<sub>20</sub>, wherein **R**<sub>20</sub> is pyridinyl, quinolyl, (lower alkyl)-pyridinyl or (lower alkyl)-quinolyl, each optionally mono-, di- or tri-substituted with **R**<sub>21</sub>,

wherein each **R**<sub>21</sub> is independently C<sub>1-6</sub> alkyl; C<sub>1-6</sub> alkoxy; lower thioalkyl; sulfonyl; NO<sub>2</sub>; OH; SH; halo; haloalkyl; amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl, C<sub>6</sub> or C<sub>10</sub> aryl, C<sub>7-14</sub> aralkyl, Het or (lower alkyl)-Het; amido optionally mono-substituted with C<sub>1-6</sub> alkyl, C<sub>6</sub> or C<sub>10</sub> aryl, C<sub>7-14</sub> aralkyl, Het or (lower alkyl)-Het; carboxyl; carboxy(lower alkyl); C<sub>6</sub> or C<sub>10</sub> aryl, C<sub>7-14</sub> aralkyl or Het, said aryl, aralkyl

or Het being optionally substituted with  $R_{22}$ ;

wherein  $R_{22}$  is  $C_{1-6}$  alkyl;  $C_{3-7}$  cycloalkyl;  $C_{1-6}$  alkoxy; amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl; sulfonyl; (lower alkyl)sulfonyl;  $NO_2$ ; OH; SH; halo; haloalkyl; carboxyl; amide; (lower alkyl)amide; or Het optionally substituted with  $C_{1-6}$  alkyl;

$R^1$  is H;  $C_{1-6}$  alkyl,  $C_{3-7}$  cycloalkyl,  $C_{2-6}$  alkenyl, or  $C_{2-6}$  alkynyl, all optionally substituted with halogen;

or a pharmaceutically acceptable salt or ester thereof;

wherein "Het" is defined as a five-membered saturated or unsaturated, aromatic or non-aromatic, heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur, wherein said heterocycle is optionally fused to a benzene ring.

44  
45.  
CS (three times amended) A compound of formula I according to claim 1, wherein **B** is a  $C_6$  or  $C_{10}$  aryl or  $C_{7-16}$  aralkyl, all optionally substituted with  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amido, or amino optionally substituted with  $C_{1-6}$  alkyl; or Het or (lower alkyl)-Het, all optionally substituted with  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amido, or amino optionally substituted with  $C_{1-6}$  alkyl, or

**B** is  $R_4-SO_2$  wherein  $R_4$  is preferably amido; (lower alkyl)amide;  $C_6$  or  $C_{10}$  aryl,  $C_{7-14}$  aralkyl or Het, all optionally substituted with  $C_{1-6}$  alkyl, or

**B** is an acyl derivative of formula  $R_4-C(O)-$  wherein  $R_4$  is

- (i)  $C_{1-10}$  alkyl optionally substituted with carboxyl, hydroxy or  $C_{1-6}$  alkoxy, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl;
- (ii)  $C_{3-7}$  cycloalkyl or  $C_{4-10}$  alkylcycloalkyl, both optionally substituted with hydroxy, carboxyl, ( $C_{1-6}$  alkoxy)carbonyl, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl;
- (iv)  $C_6$  or  $C_{10}$  aryl or  $C_{7-16}$  aralkyl, all optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with  $C_{1-6}$  alkyl;
- (v) Het or (lower alkyl)-Het, both optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amino optionally substituted with  $C_{1-6}$  alkyl, amido, (lower alkyl)amide, or amino optionally substituted with  $C_{1-6}$  alkyl, or

**B** is a carboxyl derivative of formula  $R_4-O-C(O)-$ , wherein  $R_4$  is

- (i)  $C_{1-10}$  alkyl optionally substituted with carboxyl,  $C_{1-6}$  alkanoyl, hydroxy,  $C_{1-6}$  alkoxy, amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl, amido or (lower alkyl)amide;
- (ii)  $C_{3-7}$  cycloalkyl,  $C_{4-10}$  alkylcycloalkyl, all optionally substituted with carboxyl, ( $C_{1-6}$  alkoxy)carbonyl, amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl, amido or (lower alkyl)amide;
- (iv)  $C_6$  or  $C_{10}$  aryl or  $C_{7-16}$  aralkyl optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl; or
- (v) Het or (lower alkyl)-Het, both optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl, amido or (lower alkyl)amido, or

**B** is an amide derivative of formula  $R_4-N(R_5)-C(O)-$  wherein  $R_4$  is

- (i)  $C_{1-10}$  alkyl optionally substituted with carboxyl,  $C_{1-6}$  alkanoyl, hydroxy,  $C_{1-6}$  alkoxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl;
- (ii)  $C_{3-7}$  cycloalkyl or  $C_{4-10}$  alkylcycloalkyl, all optionally substituted with carboxyl, ( $C_{1-6}$  alkoxy)carbonyl, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl;
- (iii) amino optionally mono- or di-substituted with  $C_{1-3}$  alkyl;
- (iv)  $C_6$  or  $C_{10}$  aryl or  $C_{7-16}$  aralkyl, all optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with  $C_{1-6}$  alkyl; or
- (v) Het or (lower alkyl)-Het, both optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amino optionally substituted with  $C_{1-6}$  alkyl, amido or (lower alkyl)amide; and  $R_5$  is H or methyl, or

**B** is thioamide derivative of formula  $R_4-NH-C(S)-$ ; wherein  $R_4$  is

- (i)  $C_{1-10}$  alkyl optionally substituted with carboxyl,  $C_{1-6}$  alkanoyl or  $C_{1-6}$  alkoxy;
- (ii)  $C_{3-7}$  cycloalkyl or  $C_{4-10}$  alkylcycloalkyl, all optionally substituted with carboxyl, ( $C_{1-6}$  alkoxy)carbonyl, amino or amido;

**Y** is H or methyl;

$R^3$  is  $C_{1-8}$  alkyl,  $C_{3-7}$  cycloalkyl, or  $C_{4-10}$  alkylcycloalkyl, all optionally substituted with hydroxy,  $C_{1-6}$  alkoxy,  $C_{1-6}$  thioalkyl, acetamido,  $C_6$  or  $C_{10}$  aryl, or  $C_{7-16}$  aralkyl;

$R^2$  is  $S-R_{20}$  or  $O-R_{20}$  wherein  $R_{20}$  is pyridinyl, quinolyl,  $-CH_2$ -pyridinyl or  $-CH_2$ -quinolyl, all

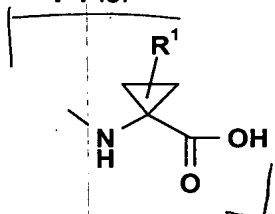
optionally mono-, di- or tri-substituted with  $R_{21}$ , wherein

$R_{21}$  is  $C_{1-6}$  alkyl;  $C_{1-6}$  alkoxy; lower thioalkyl; amino or amido optionally mono- or di-substituted with  $C_{1-6}$  alkyl,  $C_6$  or  $C_{10}$  aryl,  $C_{7-16}$  aralkyl, Het or (lower alkyl)-Het;  $NO_2$ ; OH; halo; trifluoromethyl; carboxyl;  $C_6$  or  $C_{10}$  aryl,  $C_{7-16}$  aralkyl, or Het, said aryl, aralkyl or Het being optionally substituted with  $R_{22}$ , wherein

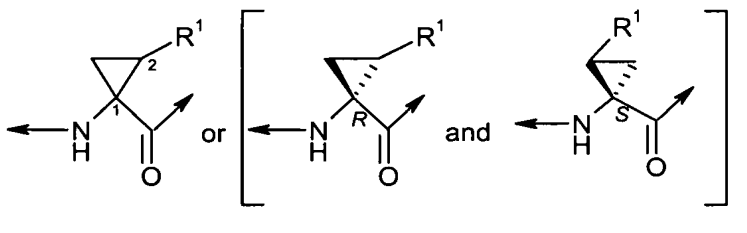
$R_{22}$  is  $C_{1-6}$  alkyl;  $C_{3-7}$  cycloalkyl;  $C_{1-6}$  alkoxy; amino; mono- or di-(lower alkyl)amino; (lower alkyl)amide; sulfonylalkyl;  $NO_2$ ; OH; halo; trifluoromethyl; carboxyl or Het;

or  $R^2$  is quinolinoxy unsubstituted, mono- or di-substituted with  $R_{21}$  as defined above; and

$P1$  is:



wherein  $R^1$  is H,  $C_{1-3}$  alkyl,  $C_{3-5}$  cycloalkyl, or  $C_{2-4}$  alkenyl optionally substituted with halo, and said  $R^1$  at carbon 2 is orientated syn to the carbonyl at position 1, represented by the radical:



or a pharmaceutically acceptable salt or ester thereof.

46. <sup>45</sup> (three times amended) A compound of formula I according to claim ~~45~~, wherein **B** is a  $C_6$  or  $C_{10}$  aryl optionally substituted with  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl; or **B** is Het optionally substituted with  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkanoyl, hydroxy, halo, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl; or **B** is  $R_4-SO_2$  wherein  $R_4$  is  $C_6$  or  $C_{10}$  aryl, a  $C_{7-14}$  aralkyl or Het all optionally substituted with  $C_{1-6}$  alkyl; amido, (lower alkyl)amide; **B** is an acyl derivative of formula  $R_4-C(O)-$

wherein **R<sub>4</sub>** is

- C5  
only
- (i) C<sub>1-10</sub> alkyl optionally substituted with carboxyl, hydroxy or C<sub>1-6</sub> alkoxy; or
  - (ii) C<sub>3-7</sub> cycloalkyl or C<sub>4-10</sub> alkylcycloalkyl, both optionally substituted with hydroxy, carboxyl, (C<sub>1-6</sub> alkoxy)carbonyl; or
  - (iv) C<sub>6</sub> or C<sub>10</sub> aryl or C<sub>7-16</sub> aralkyl, all optionally substituted with C<sub>1-6</sub> alkyl, hydroxy; or
  - (v) Het optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amido or amino;

or **B** is a carboxyl derivative of formula **R<sub>4</sub>-O-C(O)-**, wherein **R<sub>4</sub>** is

- (i) C<sub>1-10</sub> alkyl optionally substituted with carboxyl, C<sub>1-6</sub> alkanoyl, hydroxy, C<sub>1-6</sub> alkoxy or amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl;
- (ii) C<sub>3-7</sub> cycloalkyl, C<sub>4-10</sub> alkylcycloalkyl, all optionally substituted with carboxyl, (C<sub>1-6</sub> alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl; or
- (iv) C<sub>6</sub> or C<sub>10</sub> aryl or C<sub>7-16</sub> aralkyl, all optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amino optionally substituted with C<sub>1-6</sub> alkyl; or
- (v) Het or (lower alkyl)-Het, both optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amido, or amino optionally mono-substituted with C<sub>1-6</sub> alkyl;

or **B** is an amide derivative of formula **R<sub>4</sub>-N(R<sub>5</sub>)-C(O)-** wherein **R<sub>4</sub>** is

- (i) C<sub>1-10</sub> alkyl optionally substituted with carboxyl, C<sub>1-6</sub> alkanoyl, hydroxy, C<sub>1-6</sub> alkoxy, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl;
- (ii) C<sub>3-7</sub> cycloalkyl or C<sub>4-10</sub> alkylcycloalkyl, all optionally substituted with carboxyl, (C<sub>1-6</sub> alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl; and **R<sub>5</sub>** is H or methyl; or
- R<sub>4</sub>** is (iii) amino optionally mono- or di-substituted with C<sub>1-3</sub> alkyl; or
- (iv) C<sub>6</sub> or C<sub>10</sub> aryl or C<sub>7-16</sub> aralkyl, all optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amino or amido optionally substituted with C<sub>1-6</sub> alkyl; or
- (v) Het optionally substituted with C<sub>1-6</sub> alkyl, hydroxy, amino or amido; or

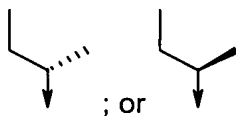
**B** is a thioamide derivative of formula **R<sub>4</sub>-NH-C(S)-**; wherein **R<sub>4</sub>** is:

- (i) C<sub>1-10</sub> alkyl; or (ii) C<sub>3-7</sub> cycloalkyl; or

**Y** is H;

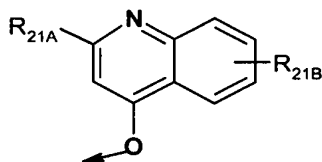
**R<sup>3</sup>** is the side chain of Tbg, Ile, Val, Chg or:

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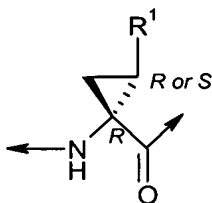
$R^2$  is quinolinoxy unsubstituted, mono- or di-substituted with  $R_{21}$  as defined above, or

$R^2$  is:



wherein  $R_{21A}$  is  $C_{1-6}$  alkyl;  $C_{1-6}$  alkoxy;  $C_6$ ,  $C_{10}$  aryl or Het; lower thioalkyl; halo; amino optionally mono-substituted with  $C_{1-6}$  alkyl; or  $C_6$ ,  $C_{10}$  aryl,  $C_{7-16}$  aralkyl or Het, optionally substituted with  $R_{22}$  wherein  $R_{22}$  is  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with  $C_{1-6}$  alkyl, or Het; and  $R_{21B}$  is  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, amino, di(lower alkyl)amino, (lower alkyl)amide,  $NO_2$ , OH, halo, trifluoromethyl, or carboxyl;

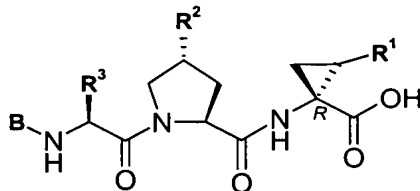
$P1$  is:



; and

$R^1$  is ethyl, vinyl, cyclopropyl, 1 or 2-bromoethyl or 1 or 2-bromovinyl.

52. (twice amended) A compound according to claim 45 represented by the formula:



wherein  $B$ ,  $R^3$ ,  $R^2$ ,  $R^1$  are as defined below:

Table 3 Cpd #	B	$R^3$	$R^2$	$R^1$ syn to carboxyl ethyl
304	Boc	cHex		

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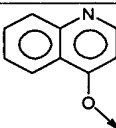
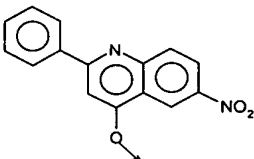
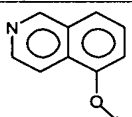
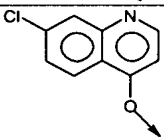
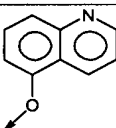
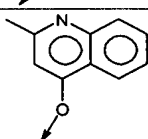
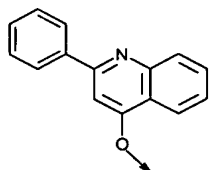
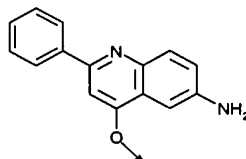
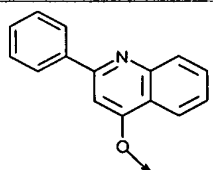
Table 3 Cpd #	B	R <sup>3</sup>	R <sup>2</sup>	R <sup>1</sup> syn to carboxyl vinyl	
306	Boc	cHex		vinyl	;
307	Boc	cHex		vinyl	;
310	Boc	cHex		vinyl	;
311	Boc	cHex		vinyl	;
312	Boc	cHex		vinyl	;
313	Boc	cHex		vinyl	;
314	Boc	cHex		vinyl	;
315	Boc	cHex		vinyl	;
316	Acetyl	cHex		vinyl	;

Table 3 Cpd #	B	R <sup>3</sup>	R <sup>2</sup>	R <sup>1</sup> syn to carboxyl	
317	Boc	cHex		vinyl	;
318	CF <sub>3</sub> -C(O)-	<i>i</i> -Pr		vinyl	;
322	Boc	<i>t</i> -Bu		vinyl	;
325	Boc	<i>t</i> -Bu			;
327		<i>t</i> -Bu		vinyl	;
328	Boc	<i>t</i> -Bu		vinyl	;
331		<i>t</i> -Bu		vinyl	;
332	Boc	<i>t</i> -Bu		ethyl	;

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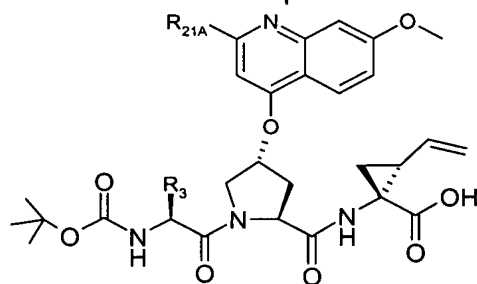


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Table 3 Cpd #	B	R <sup>3</sup>	R <sup>2</sup>	R <sup>1</sup> syn to carboxyl vinyl
333		<i>t</i> -Bu		;
and 334		<i>t</i> -Bu		.

52  
53. (twice amended) A compound according to claim 52, selected from the group consisting of compound #: 307, 314, 317, 325, 327, 331, 332, 333, and 334.

59  
60. (twice amended) A compound according to claim 46 represented by the formula:

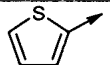
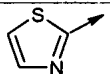
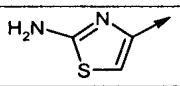
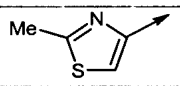
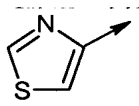
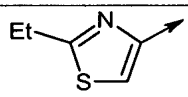
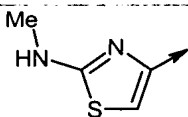
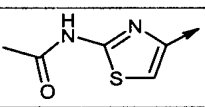
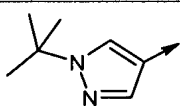
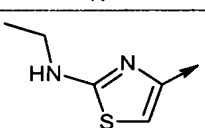
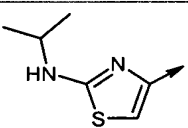
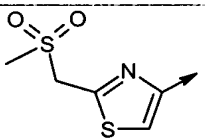


wherein R<sub>3</sub> and R<sub>21A</sub> are as defined below:

T1730

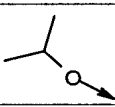
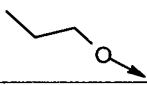
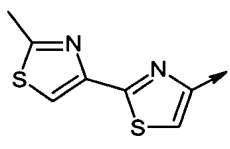
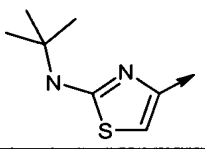
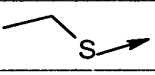
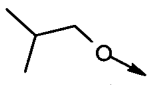
Table 7 Cpd #	R <sub>3</sub>	R <sub>21A</sub>
701	<i>t</i> -Bu	
702	<i>t</i> -Bu	
703	<i>t</i> -Bu	
704	<i>t</i> -Bu	

C7  
Amended

Table 7 Cpd #	R <sub>3</sub>	R <sub>21A</sub>	
706	<i>t</i> -Bu		;
707	<i>t</i> -Bu		;
708	<i>t</i> -Bu	Ph-N(Me)-	;
709	<i>t</i> -Bu		;
710	<i>t</i> -Bu	HOOC-	;
711	<i>t</i> -Bu		;
712	<i>t</i> -Bu	(Me) <sub>2</sub> N-	;
713	<i>t</i> -Bu		;
714	<i>t</i> -Bu		;
717	<i>t</i> -Bu		;
718	<i>t</i> -Bu	NH <sub>2</sub>	;
719	<i>t</i> -Bu		;
720	<i>t</i> -Bu		;
722	<i>t</i> -Bu		;
723	<i>t</i> -Bu		;
726	<i>t</i> -Bu	<i>i</i> -Pr	;
728	<i>t</i> -Bu		;

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C

Table 7 Cpd #	R <sub>3</sub>	R <sub>21A</sub>	
730	<i>t</i> -Bu		;
731	<i>t</i> -Bu		;
732	<i>t</i> -Bu		;
733	<i>t</i> -Bu		;
734	<i>t</i> -Bu		;
735	<i>t</i> -Bu		;
736	<i>t</i> -Bu	<i>t</i> -Bu	;
and 737	<i>t</i> -Bu	CHex	.

60 (twice amended) A compound according to claim 60, selected from the group consisting of compound #: 701, 702, 703, 704, 706, 707, 708, 709, 711 to 714, 717 to 720, 722, 723, 726, 728, and 730 to 737.

Please Cancel Claims 76-79 without prejudice. ✓

### SPECIFICATION AMENDMENTS SHOWING THE CHANGES MADE

At page 4, lines 19-21, delete the paragraph and replace with the following:

-- or B is an acyl derivative of formula R<sub>4</sub>-C(O)-; a carboxyl derivative of formula R<sub>4</sub>-O-C(O)-; an amide derivative of formula R<sub>4</sub>-N(R<sub>5</sub>)-C(O)-; a thioamide derivative of formula R<sub>4</sub>-N(R<sub>5</sub>)-C(S)-; or a sulfonyl derivative of formula R<sub>4</sub>-SO<sub>2</sub> wherein --